

REMARKS

Entry is respectfully requested of this Preliminary Amendment, which brings forward amendments that were made to the specification of parent Application Serial No. 09/219,337. This amendment cancels the claims elected in the parent application and presents claims pertaining to the non-elected invention from the parent application. Early examination on the merits respectfully is requested.

Respectfully submitted,

Date: June 6, 2001

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09/219,337

MARKED-UP COPY OF SPECIFICATION

Page 3, paragraph 3:

Figures 1(a), 1(b) and 1(c) depict **a nucleotide sequence (SEQ ID NOS 1 and 2) that corresponds with** amino acid residues 1-235 of VP26 (ORF23) (Ellen strain). This contains a total of 235 AA and has a theoretical molecular weight of 24.4 kDa. The region in bold corresponds to an AA 12 – 235 VP26* immunoreactive fragment having a total of 224 amino acids and a theoretical molecular weight of 23 kDa. The rhombus (#) symbolizes a stop codon. The numbering of the amino acids begins with a methionine start codon of the published ORF23 sequence (A.J. Davison & J.E. Scott. (1986), J. Gen. Virol. 67, 1759-1816) as shown in **this** Figure [2].

Page 4, paragraph 1

[Figure 2 shows a nucleotide sequence that corresponds with the amino acid sequence shown in Figure 1.]

Page 4, paragraph 2

Figure [3] **2** shows data obtained from an ELISA test in accordance with an embodiment of the invention.

Page 4, paragraph 3

Figure [4] **3** shows data obtained from another ELISA test in accordance with an embodiment of the invention.

Page 4, paragraph 4

[Figure 5 is a list of sequences described in the specification.]

Page 9, paragraph 2

Example 3: Cloning ORF23 (VP26)

The viral DNA (see Example 1) or the phagemid vector, pBK/CMV-23, obtained from the immunoreactive lambda phage served as a template for amplifying the ORF23 (VP26) or, respectively, the ORF23 fragment (VP26*) which was inserted in vector pBK/CMV-23. The following primers were used as amplification oligonucleotides: VP26:VP26H 5' GGAATTCCGGATGACACAACCCGCATCGTCTCGTGTA 3' (SEQ ID NO:3); VP26R 5' GCTCTAGATTACACCCTACGACTTCTTGAAGCGTTTCC 3' (SEQ ID NO:4); VP26*:VP26*H 5' GGAATTCCGCGCCTGCAGGTCGACACTAGTGGAT 3' (SEQ ID NO:5); VP26*R 5' GCTCTAGATTACACCCTACGACTTCTTGAAGCGTTTCC 3' (SEQ ID NO:4);

Page 9, paragraph 3

These oligonucleotides are complementary to the corresponding segment of the published VZV sequence (A.J. Davison & J.E. Scott. (1986), J. Gen. Virol. 67, 1759-1816) or the sequence of vector pBK/CMV (Stratagene), but they contain, at their 5' termini, a restriction cleavage site sequence which did not hybridize the template DNA. After amplification had taken place, the amplificate, of 726 bp or 714 bp in size, respectively, was cleaved terminally with the restriction enzymes EcoRI and XbaI and ligated into expression vector pMAL-c2, which had been linearized previously with EcoRI and XbaI. The entire ORF23 was completely sequenced in an overlapping,

bidirectional manner. The vectors were designated pMAL-VP26 and pMAL-VP26*, respectively.

In addition, the region (VP26*) encoding the immunoreactive protein was cloned into vector pQE30. VZV genomic DNA was used as the template DNA. The following primers were used as amplification oligonucleotides: VP26*:VP26* 5' CGGATCCGATCCCAGCAACCCCACCAC 3' (SEQ ID NO:6); VP26R 5' GCTCTAGATTACACCCTACGACTTCTTGAAGCGTTTCC 3' (SEQ ID NO:4).

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Markus EICKMANN *et al*
VARICELLA ZOSTER VIRUS (VZV)
IMMUNOREACTIVE PROTEIN VP26
AND ITS DIAGNOSTIC USE
38137-0018

Figure 2

Met Thr Gln Pro Ala Ser Ser Arg Val Val Phe Asp Pro Ser Asn Pro
Thr Thr Phe Ser Val Glu Ala Ile Ala Ala Tyr Thr Pro Val Ala Leu
Ile Arg Leu Leu Asn Ala Ser Gly Pro Leu Gln Pro Gly His Arg Val
Asp Ile Ala Asp Ala Arg Ser Ile Tyr Thr Val Gly Ala Ala Ala Ser
Ala Ala Arg Ala Arg Ala Asn His Asn Ala Asn Thr Ile Arg Arg Thr
Ala Met Phe Ala Gln Thr Asp Pro Met Thr Tyr Leu Arg Pro Thr Val
Gly Leu Lys Arg Thr Phe Asn Pro Arg Ile Ile Arg Pro Gln Pro Pro
Asn Pro Ser Met Ser Leu Gly Ile Ser Gly Pro Thr Ile Leu Pro Gln
Lys Thr Gln Ser Ala Asp Gln Ser Ala Leu Gln Gln Pro Ala Ala Leu
Ala Phe Ser Gly Ser Ser Pro Gln His Pro Pro Pro Gln Thr Thr Ser
Ala Ser Val Gly Gln Gln Gln His Val Val Ser Gly Ser Ser Gly Gln
Gln Pro Gln Gln Gly Ala Gln Ser Ser Thr Val Gln Pro Thr Thr Gly
Ser Pro Pro Ala Ala Gln Gly Val Pro Gln Ser Thr Pro Pro Pro Thr
Gln Asn Thr Pro Gln Gly Gly Lys Gly Gln Thr Leu Ser His Thr Gly
Gln Ser Gly Asn Ala Ser Arg Ser Arg Arg Val *

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VARICELLA ZOSTER VIRUS (VZV)
IMMUNOREACTIVE PROTEIN VP26
AND ITS DIAGNOSTIC USE
38137-0018

Figure 3/2

No.	Status	ELISA	ELISA	ELISA	No.	Status	ELISA	ELISA	ELISA
		IgM	IgM	IgM			IgM	IgM	IgM
		Reference	pMal- VP26*	pQE- VP26*			Reference	pMal- VP26*	pQE- VP26*
			1 µg/ml	1 µg/ml				1 µg/ml	1 µg/ml
		Conj.	Conj.	Conj.			Conj.	Conj.	Conj.
		1:50	1:50	1:25			1:50	1:50	1:25
		Serum	Serum	Serum			Serum	Serum	Serum
		1:42	1:168	1:168			1:42	1:168	1:168
1	-	11	86	62	29	-	16	19	104
2	-	22	38	100	30	-	8	13	44
3	-	16	31	72	31	-	3	23	47
4	-	57	23	88	32	-	50	23	101
5	+	133	399	88	33	-	9	32	117
6	-	0	161	118	34	+	250	187	204
7	-	10	28	77	35	+	291	1079	470
8	-	47	45	60	36	-	26	52	44
9	-	7	16	63	37	+	139	66	123
10	+	132	173	160	38	-	38	87	49
11	-	71	117	70	39	-	26	25	40
12	-	0	32	75	40	-	49	13	63
13	-	17	75	66	41	-	5	20	34
14	-	11	16	57	42	-	27	43	80
15	-	23	27	73	43	-	51	49	161
16	-	11	27	59	44	-	8	38	100
17	+	979	1720	532	45	-	21	38	133
18	-	9	18	44	46	-	10	33	82
19	-	34	30	71	47	-	29	18	35
20	+	293	630	215	48	-	30	66	97
21	+	126	139	259	49	-	21	35	97
22	-	61	277	169	50	-	56	64	82
23	+	292	808	154	51	-	5	40	56
24	+	581	98	115	52	-	97	55	37
25	+	321	821	304	53	-	2	19	35
26	+	509	519	375	54	-	31	21	39
27	+	298	>2500	694					
28	-	29	36	29					

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Figure 4

No.	Status	ELISA IgG Reference	ELISA IgG pMal VP26* 1 µg/ml	ELISA IgG pQE VP26* 2 µg/ml
		Conj. 1:50	Conj. 1:50	Conj. 1:50
		Serum 1:231	Serum 1:100	Serum 1:100
1	+	1014	176	137
2	+	302	87	356
3	+	642	97	314
4	+	612	87	0
5	+	1383	181	215
6	+	930	132	118
7	+	653	39	145
8	+	915	47	469
9	+	570	23	220
10	+	1770	131	253
11	+	990	104	76
12	+	698	227	335
13	+	141	62	501
14	+	338	39	44
15	+	556	113	246
16	+	791	45	423
17	+	2982	264	258
18	+	1205	192	295
19	+	694	80	100
20	+	1143	270	340
21	+	1405	377	256
22	+	539	42	72
23	+	2449	533	530
24	+	1923	1117	620
25	+	1420	95	54
26	Primary +	1194	277	66
27	Zoster +	2087	341	204

No.	Status	ELISA IgG Reference	ELISA IgG pMal VP26* 1 µg/ml	ELISA IgG pQE VP26* 2 µg/ml
		Conj. 1:50	Conj. 1:50	Conj. 1:50
		Serum 1:231	Serum 1:100	Serum 1:100
28	+	549	89	172
29	-	34	87	120
30	-	76	55	128
31	-	0	38	101
32	-	41	94	116
33	-	8	147	177
34	+	1315	860	340
35	+	1629	282	187
36	+	469	218	287
37	+	693	181	346
38	+	1449	296	169
39	+	1139	85	193
40	+	1509	64	118
41	+	457	110	159
42	+	343	304	545
43	+	1455	511	244
44	+	1030	174	245
45	+	528	50	184
46	+	510	161	353
47	+	300	94	290
48	+	490	91	157
49	+	888	348	277
50	+	1301	83	195
51	+	704	247	139
52	+	2523	2325	757
53	+	447	99	153
54	+	848	149	167

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VARICELLA ZOSTER VIRUS (VZV)
IMMUNOREACTIVE PROTEIN VP26
AND ITS DIAGNOSTIC USE
38137-0018

Figure 5

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:

- (A) NAME: Dade Behring Marburg GmbH
- (B) STREET: Emil-von-Behring Str. 76
- (C) CITY: Marburg
- (E) COUNTRY: Germany
- (F) POSTAL CODE (ZIP): 35001 Marburg
- (G) TELEPHONE: 06421/39-2332
- (H) TELEFAX: 06421/39-3631

- (ii) TITLE OF INVENTION: Immunreaktives Protein VP26 des
Varicella-Zoster-Virus (VZV) und seine diagnostische
Verwendung

- (iii) NUMBER OF SEQUENCES: 8

(iv) COMPUTER READABLE FORM:

- (A) MEDIUM TYPE: Floppy disk
- (B) COMPUTER: IBM PC compatible
- (C) OPERATING SYSTEM: PC-DOS/MS-DOS
- (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(v) CURRENT APPLICATION DATA:

APPLICATION NUMBER: DE 19757765.2

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 235 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein

- (iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Varicella-Zoster-Virus
- (B) STRAIN: Ellen

(vii) IMMEDIATE SOURCE:

- (B) CLONE: VP26

(viii) POSITION IN GENOME:

- (B) MAP POSITION: ORF23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

Met Thr Gln Pro Ala Ser Ser Arg Val Val Phe Asp Pro Ser Asn Pro

105090-0474850

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VARICELLA ZOSTER VIRUS (VZV)
IMMUNOREACTIVE PROTEIN VP26
AND ITS DIAGNOSTIC USE
38137-0018

1 5 10 15

Thr Thr Phe Ser Val Glu Ala Ile Ala Ala Tyr Thr Pro Val Ala Leu
20 25 30

Ile Arg Leu Leu Asn Ala Ser Gly Pro Leu Gln Pro Gly His Arg Val
35 40 45

Asp Ile Ala Asp Ala Arg Ser Ile Tyr Thr Val Gly Ala Ala Ala Ser
50 55 60

Ala Ala Arg Ala Arg Ala Asn His Asn Ala Asn Thr Ile Arg Arg Thr
65 70 75 80

Ala Met Phe Ala Glu Thr Asp Pro Met Thr Trp Leu Arg Pro Thr Val
85 90 95

Gly Leu Lys Arg Thr Phe Asn Pro Arg Ile Ile Arg Pro Gln Pro Pro
100 105 110

Asn Pro Ser Met Ser Leu Gly Ile Ser Gly Pro Thr Ile Leu Pro Gln
115 120 125

Lys Thr Gln Ser Ala Asp Gln Ser Ala Leu Gln Gln Pro Ala Ala Leu
130 135 140

Ala Phe Ser Gly Ser Ser Pro Gln His Pro Pro Pro Gln Thr Thr Ser
145 150 155 160

Ala Ser Val Gly Gln Gln Gln His Val Val Ser Gly Ser Ser Gly Gln
165 170 175

Gln Pro Gln Gln Gly Ala Gln Ser Ser Thr Val Gln Pro Thr Thr Gly
180 185 190

Ser Pro Pro Ala Ala Gln Gly Val Pro Gln Ser Thr Pro Pro Pro Thr
195 200 205

Gln Asn Thr Pro Gln Gly Gly Lys Gly Gln Thr Leu Ser His Thr Gly
210 215 220

Gln Ser Gly Asn Ala Ser Arg Ser Arg Arg Val
225 230 235

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 705 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: YES

109090-0442850

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VARICELLA ZOSTER VIRUS (VZV)
IMMUNOREACTIVE PROTEIN VP26
AND ITS DIAGNOSTIC USE
38137-0018

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Varicella-Zoster-Virus
(B) STRAIN: Ellen

(viii) POSITION IN GENOME:

- (B) MAP POSITION: ORF23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

ATGACACAAC CCGCATCGTC TCGTGTAGTC TTTGATCCCA GCAACCCCAC
CACATTTTCG 60

GTGGAAGCAA TTGCGGCTTA CACCCCGTT GCTTTAATAC SACTTTTAAA
CGCCAGTGGA 120

CCTTTGCAAC CTGGTCACCG TGTGGACATC GCTGATCCCA GAAGCATTTA
CACCGTGGGA 180

GCCGCGGCCA GTGCCGCGCG TGCACGCGCT AACCATAATG CAAATACGAT
ACGCCGAACG 240

GCCATGTTTG CCGAGACTGA CCCTATGACA TGGTTAAGAC CAACGGTTGG
CTTAAACGT 300

ACGTTTAACC CGCGTATTAT ACGACCACAA CCCCCAAATC CATCCATGAG
TTTGGAATC 360

TCGGGGCCTA CTATATTGCC GCAAAAAACA CAGAGCGCCG ATCAGTCTGC
TTTACAACAG 420

CCCGCCGCGT TGGCGTTTTT GGGATCATCG CCGCAACACC CCCCACCTCA
AACGACGTCG 480

GCATCCGTTG GACAACAGCA ACACGTGGTG TGGGGTCTT CTGGACAACA
ACCGCAACAG 540

GGAGCACAGT CAAGCACTGT CCAGCCAACA ACCGGATCAC CGCCCGCGGC
CCAAGGCGTG 600

CCACAGTCTA CCCC GCCCCC AACCCAAAAT ACCCCCCAGG GGGGTAAGGG
ACAGACCTTG 660

TCACACACGG GACAATCTGG AAACGCTTCA AGAAGTCGTA GGGTG
705

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 37 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

109030-047850

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VARICELLA ZOSTER VIRUS (VZV)
IMMUNOREACTIVE PROTEIN VP26
AND ITS DIAGNOSTIC USE
38137-0018

(A) DESCRIPTION: /desc = "Synthetische DNA"

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Varicella-Zoster-Virus

(B) STRAIN: Ellen

(viii) POSITION IN GENOME:

(B) MAP POSITION: ORF23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

GGAATTCGG ATGACACAAC CCGCATCGTC TCGTGTA

37

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 38 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "Synthetische DNA"

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Varicella-Zoster-Virus

(B) STRAIN: Ellen

(viii) POSITION IN GENOME:

(B) MAP POSITION: ORF23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

GCTCTAGATT ACACCCTACG ACTTCTTGAA GCGTTTCC

38

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "Synthetische DNA"

(iii) HYPOTHETICAL: NO

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VARICELLA ZOSTER VIRUS (VZV)
IMMUNOREACTIVE PROTEIN VP26
AND ITS DIAGNOSTIC USE
38137-0018

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Varicella-Zoster-Virus
(B) STRAIN: Ellen

(viii) POSITION IN GENOME:
(B) MAP POSITION: ORF23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:
GGAATTCCGC GCCTGCAGGT CGACACTAGT GGAT

34

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "Synthetische DNA"

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Varicella-Zoster-Virus
(B) STRAIN: Ellen

(viii) POSITION IN GENOME:
(B) MAP POSITION: ORF23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:
GCTCTAGATT ACACCCCTACG ACTTCTTGAA GCGTTTCC

38

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "Synthetische DNA"

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Varicella-Zoster-Virus
(B) STRAIN: Ellen

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Markus EICKMANN *et al*
VARICELLA ZOSTER VIRUS (VZV)
IMMUNOREACTIVE PROTEIN VP26
AND ITS DIAGNOSTIC USE
38137-0018

(viii) POSITION IN GENOME:
(B) MAP POSITION: ORF23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

CGGATCCGAT CCCAGCAACC CCACCAC

27

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 38 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: ?desc = "Synthetische DNA"

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Varizella-Zoster-Virus
- (B) STRAIN: Ellen

(viii) POSITION IN GENOME:
(B) MAP POSITION: ORF23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

GCTCTAGATT ACACCCTACG ACTTCTTGAA GCGTTTCC

38

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